Risk Assessment of Ambient Ozone Concentrations Found in North Carolina

Prepared by Occupational and Environmental Epidemiology Branch
Medical Evaluation and Risk Assessment Unit
North Carolina Division of Public Health
North Carolina Department of Health and Human Services
November 1, 1999

Synopsis

The North Carolina Department of Health and Human Services (DHHS) is concerned about the public health risks to North Carolinians from exposure to environmental ozone concentrations typically seen during the summer months. Based on review of the scientific literature including United States Environmental Protection Agency (US EPA) documents, the general population and, in particular, individuals with underlying pulmonary conditions are at risk of developing respiratory problems following prolonged exposure to elevated levels of ozone that may be present during the summer months.

Ozone is one of the criteria pollutants identified by the US EPA under the Clean Air Act of 1970. A level of 0.12 parts per million (ppm) 1-hour average was set as the primary standard <u>to protect the public health</u> including the health of sensitive populations, and was set as a secondary standard to protect public welfare, damage to crops, animals, and buildings. Since the standard was developed, US EPA has reviewed more than 3,000 studies and is proposing to phase out the previous 1-hour primary ozone standard of 0.12 parts per million (promulgated in 1997) and replace it with an 8-hour standard of 0.08 ppm. It is estimated that compliance with this new standard will significantly decrease ozone-related emergency room and physician visits, and hospital admissions associated with respiratory problems (such as asthma attacks and pulmonary infections). The US EPA also proposes to replace the secondary ozone standard of 0.12 ppm (1-hour average) with a standard identical to the proposed primary standard of 0.08 ppm. With the new secondary standard, the US EPA estimates a reduction in agricultural crop losses by almost 500 million dollars.

After review of the US EPA's Ozone Criteria Document and Office of Air Quality Planning and Standards Staff Paper and other medical literature, the Medical Evaluation and Risk Assessment (MERA) Unit of the Occupational and Environmental Epidemiology Branch in the Division of Public Health concurs with the justification of the US EPA to establish the new primary ozone standard at 0.08 parts per million (ppm) over an 8-hour time interval as opposed to using the 1-hour average standard of 0.12 ppm. The following health assessment provides support for the use of the new US EPA 8-hour standard and may be used to inform the public of the precautions that should be taken to minimize the risk of developing adverse effects from ozone exposure.

Formation of Ozone

Ozone is a reactive oxidant gas formed in the atmosphere by the chemical reaction of volatile organic compounds (VOCs) and nitrogen oxides (NOx) in the presence of sunlight (National Research Council 1991). It is a major component of smog present in the ground level atmosphere (troposphere). In contrast, the ozone layer in the stratosphere located approximately 10 km above the earth's surface serves to protect us from exposure to harmful levels of ultraviolet light (Chapman 1930 and Crutzen 1970). Major sources of NOx and VOC emissions are from cars, trucks, power plants, and factories (US EPA 1993). In certain regions of the country, especially the Southeast, natural vegetation may also produce substantial amounts of VOCs (US EPA 1996a, US EPA 1996b).

North Carolina Ozone Air Awareness Program

In North Carolina, ozone concentrations are measured during the months of April through October by the Division of Air Quality (DAQ) located in the Department of Environment and Natural Resources (DENR). There are currently 43 ozone monitoring sites throughout the state. In addition, the DAQ forecasts ozone levels for each upcoming day using meteorological and non-meteorological data. The ozone forecast for the next day is issued at 3:00 pm in order to provide sufficient lead time to get the message to the public so that necessary precautions can be taken. These forecasts are reported to the Associated Press, television and radio stations and newspapers in the Research Triangle and Charlotte areas. The Forsyth County Environmental Affairs Department informs the media in the Triad. If DAQ predicts that the ozone levels may exceed the 8-hour ozone standard of 0.08 ppm, specific state agencies are notified. The DAQ forecast can be found on the Internet at http://daq.state.nc.us. General information about ozone can be found at the US EPA web address http://www.epa.gov/airnow.

The forecast for the next day includes a specific color code which corresponds to a range of ozone concentrations predicted for that day, a US EPA derived Air Quality Index (AQI), and health advice associated with that code (US EPA 1999a). The higher the AQI, the greater the health concern. A list of these codes and summarized health effects and advice associated with each code can be found in Table 1.

Table 1. US EPA Color Codes Corresponding to Ground Level Ozone Concentrations (US EPA 1999b with modifications)

AIR QUALITY CATEGORY	**0ZONE 8-HR (ppm)**	**Air Quality Index (AQI)**	**COLOR CODE**	**HEALTH EFFECTS AND ADVICE**
GOOD	0.0-0.064	0-50	GREEN	No adverse health effects expected
MODERATE	0.065-0.084	51-100	YELLOW	Unusually sensitive groups - possible cough and painful breathing -consider limiting prolonged outdoor exposure -minimize outdoor exposure 2:00 pm to 6:00 pm
UNHEALTHY FOR SENSITIVE GROUPS	0.085-0.104	101-150	ORANGE	Sensitive groups (i.e., children, adults active outdoors, people with respiratory disease, people unusually susceptible) -possible cough, painful breathing, and ⇓ lung function -should limit prolonged outdoor exposure -minimize outdoor exposure 2:00 pm to 6:00 pm
UNHEALTHY	0.105-0.124	151-200	RED	Sensitive groups - probable cough, painful breathing, and ⇓ lung function -avoid prolonged outdoor exposure -minimize outdoor exposure 2:00 pm to 6:00 pm Healthy population -possible cough, painful breathing, and ⇓ lung function -limit prolonged outdoor exposure -minimize outdoor exposure 2:00 pm to 6:00 pm
VERY UNHEALTHY	0.125	201-300	PURPLE	Sensitive and healthy individuals likely to experience moderate to severe effects like cough, painful and impaired breathing, and ⇓ lung function Sensitive groups -avoid outdoor activity Healthy population -limit outdoor exertion -avoid outdoor exposure 2:00 pm to 6:00 pm

Environmental Ozone Concentrations

Ambient levels of ozone vary from area to area, with the time of day, with the mix of ozone-forming precursor compounds, and with the weather conditions. The estimated daytime, summer seasonal, 8-hour average background level for ozone for the United States is 0.025 to 0.045 ppm (Altshuller and Lefohn 1996). According to the North Carolina Division of Air Quality, ambient ozone levels in North Carolina are usually lowest in the early morning, while peak ozone concentrations occur typically in the early afternoon, between 2:00 pm and 6:00 pm EDT during the months of June through August, when temperatures are expected to be the highest. In contrast, along North Carolina mountain slopes and coastal areas, peak ozone concentrations often occur after 7:00 pm and the magnitude of difference between the daily low and high is smaller. This is a consequence of mountain breezes that blow steadily upslope in the daytime and steadily downslope at night and sea breezes that blow steadily inland in the daytime and out to the sea at night (Cornelius 1999).

In North Carolina, ozone levels tend to be the highest in urban areas such as Charlotte, Raleigh, Durham, Greensboro, Winston-Salem, and Fayetteville. In addition, high levels have been found in the Great Smoky Mountains. The mean and maximum 1-hour and 8-hour average concentrations reported during the hottest time of the day during June through August 1998 are listed in Table 2. The number of calendar days exceeding the US EPA 1-hour standard of 0.12 ppm and 8-hour standard of 0.08 ppm for major urban areas in North Carolina is shown in Table 3. The data found in Tables 2 and 3 were retrieved and summarized from the US EPA Aerometric Information Retrieval System (AIRS/AQS) database using daytime one-hour ozone concentrations collected during June, July and August 1998 (USEPA 1989, US EPA 1999a, Cornelius 1999).

Table 2. Mean and maximum 1-hour and 8-hour average concentrations reported during the hottest time of the day during June through August 1998 in major urban areas in North Carolina (US EPA 1989, US EPA 1999a, Cornelius 1999).

Urban Areas	Ozone Concentrations Reported in NC Metropolitan Areas (ppm)			
	Mean -1hr (2:00 - 6:00pm)	**Max.-1hr (2:00 - 6:00pm)**	**Mean-8hr (11:00am - 7:00pm)**	**Max.-8hr (11:00am - 7:00pm)**
Charlotte	0.069	0.140	0.066	0.115
Raleigh	0.068	0.132	0.066	0.119
Durham	0.066	0.130	0.063	0.102
Greensboro	0.065	0.122	0.062	0.102
Winston-Salem	0.063	0.120	0.061	0.098
Fayetteville	0.066	0.112	0.064	0.104

Table 3. Number of calendar days exceeding the US EPA 1-hour standard of 0.12 ppm and 8-hour standard of 0.08 ppm for urban areas in North Carolina in 1998 (Cornelius 1999)

Urban Areas	Number of Calendar days (June-Aug) Exceeding 0.12 ppm (1-hour standard)	Number of Calendar days (June-Aug) Exceeding 0.08 ppm (8-hour standard)
Charlotte	3	32
Raleigh	1	24
Durham	1	15
Greensboro	0	11
Winston-Salem	0	10
Fayetteville	0	15

Recently, concern has been raised regarding ozone levels indoors. Indoor ozone concentrations expressed as a percentage of outdoor ozone concentrations vary from <10 to 80% ((US EPA 1996a, Weschler et al 1989, Morrison et al 1997). This large variability is associated with many factors such as air infiltration or exchange rate of the structure, interior air circulation, interior surface composition (e.g., rugs, draperies, furniture, etc.), and reaction with other indoor air compounds. In situations where there is an indoor ozone source, such as ozone-generating air cleaners, indoor ozone concentrations have been reported to range between 0.12 to 0.80 ppm (US EPA 1998).

While the indoor ozone sources (e.g. ozone generators, electrostatic air cleaners, photocopiers, and laser printers) can be responsible for higher concentrations indoors, the literature seems to indicate that in most buildings outdoor ozone is the major source of indoor ozone. Based on the indoor to outdoor ozone ratio (<10% to 80%) reported in the literature, it appears that during certain time periods (code red and higher days) that indoor ozone exposure may be of concern in certain building environments. Of particular concern may be urban buildings, occupied by sensitive populations, that are not air-conditioned or those that have high volumes of outside air intake. However, when ozone levels outdoors are elevated, it is probably safer to be indoors if no indoor ozone sources are present.

Other Agency Guidelines for Exposure to Ozone

Other agencies have also established exposure levels for ozone. The American Conference of Governmental Industrial Hygienists (ACGIH) has established threshold limit values (TLV) for worker exposure to a number of chemical and physical agents (ACGIH 1999). The ACGIH TLV for ozone is based upon work activity. For heavy work, the TLV time-weighted average (8-hour TWA) is 0.05 ppm, for moderate work 0.08 ppm, and for light work 0.10 ppm. For work (heavy, moderate or light) of less than or equal to two hours, the excursion limit TLV is up to 0.20 ppm. The Occupational Safety and Health Administration (OSHA) has established a Permissible Exposure Limit (PEL) of 0.1 ppm 8-hour exposure, while the National Institute for Occupational Safety and Health (NIOSH) has established a Recommended Exposure Level (REL) of 0.1 ppm as a ceiling limit for ozone (US Department of Health and Human Services 1997). Guidelines set by OSHA, NIOSH, and ACGIH are meant to protect the working population, while EPA levels are set to protect the most sensitive groups in the general population.

Toxicology and Adverse Health Effects of Ozone

The toxicology and health effects from exposure to ozone have been well researched. Ozone is highly reactive and insoluble in water. The mechanisms by which ozone produces health effects are complex and various. Ozone reacts with fatty acids, sulfhydryl, amino and other electron-rich compounds in the body; can form free radicals; and increases release of arachidonic acid (Mustafra 1990, Leikauf et al 1993, US EPA 1996a, US EPA 1996b). Exposure to elevated ozone concentrations can disrupt the barrier function of the lung and may cause alterations in mucociliary bronchoalveolar clearance, function of alveolar macrophages, and immunologic competence (Gilmour et al 1993a, Gilmour et al 1991, US EPA 1996a, and US EPA 1996b). These effects can cause an increase in susceptibility to bacterial respiratory infections and can cause decrements in lung function. Ozone's potential as a carcinogen is uncertain (NTP 1994, US EPA 1996a, US EPA 1996b)

The majority of studies on health effects from ozone have focused on the effects on the pulmonary system (US EPA 1996a, US EPA 1996b, and Tepper 1994). Studies have shown that as the concentration of ozone increases, the effects on the pulmonary system are more pronounced. The various respiratory symptoms reported to occur following ozone exposure include cough, nasal irritation, throat irritation, chest pain with deep inspiration, nausea, shortness of breath, and decreased exercise performance. Objective pulmonary findings from ozone exposure include tachypnea, an increase in airways resistance, and reduction in other measures of pulmonary function such as forced expiratory flow in one second (FEV_1) and in the forced vital capacity (FVC). Ozone also causes increased airways responsiveness and increased sensitivity to allergens (US EPA 1996a, US EPA 1996b).

Healthy Individuals

The risk of developing health effects is dependent on the exposure concentration, duration of exposure, sensitivity of the individual, and activity during the time of exposure (US EPA 1996). For example, exercise increases the inhalation of ozone by increasing ventilation rate, tidal volume, inspiratory flow and thus the intrapulmonary concentration. Studies have shown that the forced expiratory volume in one second (FEV_1) decreases by 0.5 ml for every 1 part per billion (ppb) ozone exposure (Spektor et al 1988). The influences of duration and level of outdoor activity can be seen in Tables 4 and 5. In Table 4, statistically significant decrements in group mean FEV_1 (>5%

decrease in FEV_1) have been reported in healthy individuals over 8 years of age (after a few hours of exposure to ozone) when compared to controls. The decreased lung function observed in these healthy individuals was short-term and reversible. However, it is unknown if repeated short-term damage from ozone exposure could permanently injure the lungs (US EPA 1996a, USEPA 1996b, Folinsbee et al 1978, McDonnell et al 1983, Folinsbee at al 1984, Kulle et al 1985, Folinsbee et al 1988).

Table 4. Ozone Concentrations Associated with a >5% decrease in FEV_1 in Healthy Subjects (US EPA 1996a, USEPA 1996b, Folinsbee et al 1978, McDonnell et al 1983, Folinsbee at al 1984, Kulle et al 1985, Folinsbee et al 1988)

Ozone Concentration (ppm)	Duration of Activity	Level of Activity
0.08	5-6 hours	Moderate exercise
0.10	4-5 hours	Moderate exercise
0.12	3 hours	Moderate exercise
>0.16	1-3 hours	Very heavy exercise
>0.18	1-3 hours	Heavy exercise
>0.30	1-3 hours	Moderate exercise
>0.37	1-3 hours	Light exercise
>0.50	1-3 hours	Rest

Table 5. Ozone Concentrations Associated with Adverse Health Effects in Healthy Individuals
(US EPA 1996a, US EPA 1996b, McDonnell et al 1983, Folinsbee et al 1988, Avol et al 1983, Horstman et al 1990)

Ozone Concentrations (ppm)	Duration and Type of Activity	Health Effect
0.08	6.6 hours/moderate exercise	-respiratory symptoms -increases in nonspecific airways responsiveness -increases in lung lavage protein content and polymorphonuclear cells -decreased function of lung macrophages
0.12	1-3 hours/ heavy exercise	-cough
0.12	8 –hour average/moderate exercise	-temporary moderate lung function impairment in 50% of individuals exposed
0.12	8 –hour average/moderate exercise	-temporary large lung function impairment in 20% of individuals exposed
0.12	8 –hour average/moderate exercise	-temporary moderate to severe respiratory symptoms in 10-15% of individuals exposed
0.16 –0.18	1-3 hours/heavy exercise	-shortness of breath -chest pain on deep inspiration -lower respiratory scores
0.18	1-3 hours/heavy exercise	-increase in nonspecific airways responsiveness
0.4	1-3 hours/rest	-increase in nonspecific airways responsiveness

According to US EPA for many locations across the United States when a 1-hour average ozone concentration of 0.12 ppm is detected, an 8-hour average ozone concentration of 0.10 ppm is often found. As shown in Table 5, exposure to 0.12 ppm (existing 1 hour standard) for 1 to 3 hours has been associated with adverse health effects in healthy individuals and exposure to 0.08 ppm (proposed 8 hour standard) for 6.6 hours has been associated with adverse health effects in healthy individuals. In addition, the risk of developing adverse respiratory effects is higher when sensitive individuals are exposed to an 8-hour ozone concentration above 0.10 ppm. As shown in Tables 2, 4, and 5, ozone levels reported for many North Carolina urban areas have been associated with adverse health effects in healthy individuals in other parts of the United States.

Sensitive Individuals

Sensitive individuals are defined as individuals that may be more vulnerable to the effects of ozone either due to underlying physiological abnormalities or because they have a higher level of exposure due to outdoor work activities. The EPA defines four sensitive groups as (US EPA 1996a, US EPA 1996b):

- children,
- adults who are active outdoors,
- people with respiratory disease such as asthma, and
- people with unusual susceptibility to ozone (5-20% of healthy test subjects).

The health effects of ozone exposure experienced by sensitive and healthy individuals are similar, but sensitive individuals may develop responses at lower ozone concentrations or with shorter exposure duration. In some cases, the effects may be more pronounced in sensitive individuals. Respiratory health effects are rarely noticed even in sensitive individuals exposed to ozone concentrations below 0.06 ppm over an 8-hour average (US EPA 1996b). The risk of developing adverse respiratory effects is much higher when sensitive groups are exposed to an 8-hour ozone concentration above 0.10 ppm. Ozone levels reported for many North Carolina urban areas have been associated with adverse health effects in sensitive individuals in other parts of the United States.

Persons with underlying pulmonary disease are particularly at risk of developing respiratory problems following exposure to high levels of ozone and may require medical attention after ozone exposure. Ozone air pollution has been reported to be associated with an increase in hospital visits related to asthma, pneumonia, and other respiratory diseases. This was reported for several areas in the United States, Canada, and Mexico as shown in Table 6 (US EPA 1997, Steenland and Savitz 1997). It is estimated that for every million persons exposed to ambient ozone concentrations of 0.100 ppm, an additional 1-3 hospitalizations from respiratory illness occur (US EPA 1996b).

Table 6. Locations where Ozone Pollution has been reported to be Associated with Increase in Number of Hospital Visits and Admissions

Locations	Hospital Visits and Admissions
Northeastern United States	10-20% increase in hospital respiratory visits and admissions (US Dept. of Health and Human Services 1997)
Ontario, Canada	Increased frequency of hospital and emergency department visits(Steenland and Savitz 1997)
New Jersey and Mexico City	Increased frequency of hospital visits for asthma (Steenland and Savitz 1997)
New York	Increased frequency of hospital admissions for respiratory causes (Steenland and Savitz 1997)
St. Paul, Minnesota and Birmingham, Alabama	Increased hospital admissions for pneumonia (Steenland and Savitz 1997)

The Centers for Disease Control and Prevention has recently completed a survey on childhood asthma which found that 13.7 million persons in the U.S. have self-reported asthma (US Dept. of Health and Human Services 1998). State-specific prevalence rates ranged from 5.8-7.2%. Children represent 25% of the population but comprise 40% of the asthma cases. In a recent survey conducted among some North Carolina 7th and 8th graders, an asthma prevalence rate of 30% was reported (Music 1999). Because children are more likely to exercise outdoors than adults and comprise 40% of asthma cases nationwide, a high percentage of children may report symptoms associated with ozone exposure.

Public Education on Ozone Health Risks

The DHHS is concerned that ozone health risk information is not reaching city/county recreational programs, schools, day care centers, parks and camp sites where people would be engaged in outdoor activities usually during the season when ozone levels would be predicted to be the highest. The DHHS is also concerned that the media may be reporting inaccurate data. For example, during the week of June 7, 1999, the Raleigh News and Observer reported good air quality (green code) on days when the DAQ was posting orange or red codes.

The DHHS believes that more groups of individuals would benefit from a better outreach program. The DHHS feels that additional state agencies need to be involved in this educational effort. Some suggestions are listed below:

1. The Medical Evaluation and Risk Assessment (MERA) Unit of DHHS should be a resource for inquiries from the public or news media regarding the health effects from ozone exposure.

2. The DAQ (DENR), the Department of Public Instruction (DPI), and the DHHS should collaborate in developing health-related information that can be utilized by the public, school officials (i.e., school nurses, teachers, and principals) and news media. This health information may be provided in the form of brochures, fact sheets, and information included in the news media articles or on the DAQ website.

3. DHHS should provide information to North Carolina Medical Society to educate physicians on the hazards associated with ozone exposure.

4. DENR and DAQ should identify agencies that may benefit from knowledge of ozone levels to protect the public as well as their employees. Such agencies may include NC Aquariums, Forest Resources, Parks and Recreation, NC Zoological Park, and the Wildlife Commission.

5. A copy of this paper should be provided to the Department of Labor's Occupational Safety and Health Division to inform them of the hazards from ozone exposure.

6. DHHS should, in collaboration with DAQ, work with the Department of Agriculture, Department of Transportation, and Office of State Personnel to inform workers of the adverse effects from exposure to elevated ozone concentrations.

7. Explore the possibility of collaboration on indoor ozone exposure research between DHHS, DAQ and universities.

Summary

In conclusion, after reviewing various scientific documents on the health effects of ozone, the DHHS agrees with the EPA recommendation of changing the primary ambient air standard for ozone from 0.12 ppm 1-hour average to an 8-hour average of 0.08 ppm. It has been shown that sensitive individuals with pulmonary disease are at increased risk of adverse health effects from exposure to ozone. Studies have shown that sensitive individuals are likely to develop respiratory symptoms and are more likely to be hospitalized when exposed to the current 0.12 ppm 1-hour average standard. Achieving the proposed 8-hour 0.08 ppm standard should result in decreased physician visits, hospitalizations, and use of respiratory medications. In addition, some healthy individuals may experience adverse health effects to ozone at the current 1-hour average standard. Therefore, the current 1-hour standard of 0.12 ppm provides little or no margin of safety for the public, particularly for sensitive individuals.

In order to avoid unhealthy exposure to ozone, people should take the necessary precautions to minimize exposure during 2:00 to 6:00 pm when ozone levels are reported to be the highest. This is especially important for sensitive individuals like children, adults who are active outdoors, people with respiratory disease such as asthma, and people with unusual susceptibility to ozone.

The DHHS encourages the DAQ to use the 8-hour standard for ozone of 0.08 ppm, to continue ambient monitoring of ozone, and to evaluate new technologies to control volatile organic compounds and nitrogen oxide emissions in order to protect the public health. The DHHS plans to collaborate with the Division of Air Quality and other agencies to communicate the health risks associated with ozone exposure.

References

ACGIH (1999). TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents. Approved by the ACGIH Board of Directors on March 1, 1988.

Altshuller, A P, Lefohn A S (1996). Background ozone in the planetary boundary layer over the United States. J. Air Waste Manage. Assoc. 46:134-141.

Avol E L, Linn WS, Shamoo DA, Venet TG, Hackney J D (1983). Acute respiratory effects of Los Angeles smog in continuously exercising adults. J. Air Pollut. Control Assoc. 33:1055-1060.

Chameides W L, Fehsenfeld F, Rodgers M O, Cardelino C, Martinez J, Parrish D, Lonneman W, Lawson D R, Rasmussen R A, Zimmerman P, Greenberg J, Middleton P, Wang T (1992). Ozone precursor relationships in the ambient atmosphere. J. Geophys. Res. [Atmos.] 97:6037-6055.

Chapman S (1930). A theory of upper-atmospheric ozone. Mem. R. Meteorol. Soc. 3:103-125.

Crutzen P J (1970). The influence of nitrogen oxides on the atmospheric ozone content. Q. J. R. Meteorol. Soc. 96:320-325.

Cornelius WL (1999). Report from statistician with Division of Air Quality, North Carolina Department of Environment and Natural Resources.

Folinsbee LJ, Drinkwater BL, Bedi J F, Horvath SM (1978). The influence of exercise on the pulmonary function changes due to exposure to low concentrations of ozone. In: Folinsbee L J, Wagner JA, Borgia JF, Drinkwater BL, Gliner JA, Bedi JF, eds. Environmental stress: individual human adaptations. New York, NY: Academic Press; pp. 125-145.

Folinsbee LJ, Bedi JF, Horvath SM (1984). Pulmonary function changes after 1 h continuous heavy exercise in 0.21 ppm ozone. J. Appl. Physiol.: Respir. Environ. Exercise Physiol. 57:984-988.

Folinsbee LJ, McDonnell WF, Horstman,DH (1988). Pulmonary function and symptom responses after 6.6-hour exposure to 0.12 ppm ozone with moderate exercise. JAPCA 38:28-35.

Gilmour MI, Hmieleski RR, Stafford EA, Jakab GJ (1991). Suppression and recovery of the alveolar macrophage phagocytic system during continuous exposure to 0.5 ppm ozone. Exp. Lung Res. 17:547-558.

Gilmour MI, Park P, Selgrade MK (1993). Ozone-enhanced pulmonary infection with *Streptococcus zooepidemicus* in mice. Am. Rev. Respir. Dis. 147:753-760.

Horstman DH, Folinsbee LJ, Ives PJ, Abdul-Salaam S, McDonnel WF (1990). Ozone concentration and pulmonary response relationships for 6.6-hour exposures with five hours of moderate exercise to 0.08, 0.10, and 0.12 ppm. Am. Rev. Respir. Dis. 142:1158-1163.

Kulle TJ, Sauder LR, Hebel JR, Chatham MD (1985). Ozone response relationships in healthy nonsmokers. Am. Rev. Respir. Dis. 132:36-41.

Leikauf GD, Zhao Q, Zhou S, Santrock J (1993). Ozonolysis products of membrane fatty acids activate eicosanoid metabolism in human airway epithelial cells. Am. J. Respir. Cell Mol. Biol. 9:594-602

McDonnell WF, Horstman DH, Hazucha MJ, SealE., Jr., Haak ED, Salaam SA, House DE (1983). Pulmonary effects of ozone exposure during exercise: dose-response characteristics. J. Appl. Physiol.: Respir. Environ. Exercise Physiol. 54:1345-1352.

Morrison GC, Nazaroff WW (1997). Ozone Removal in Ventilation Systems Ducts, air & Waste Management Association s, Proceeding to Engineering Solutions to Indoor Air Quality Problems.

Music S (1999). Asthma surveillance in NC: Results of an ISAAC Pilot. Presentation presented by Dr. Stan Music with the North Carolina Division of Public Health.

Mustafra, MG (1990). Biochemical basis of ozone toxicity. Free Radic. Biol. Med. 9:245-265.

National Research Council (1991). Rethinking the ozone problem in urban and regional air pollution. Washington, DC: National Academy Press.

National Toxicology Program (1994). NTP technical report on the toxicology and carcinogenesis studies of ozone (CAS no. 10028-15-6) and ozone/NNK (CAS no. 10028-15-6/64091-91-4) in F344/N rats and B6C3F$_1$ mice (inhalation studies). Research Triangle Park, NC: U.S. Department of Health and Human Services, National Institutes of Health; publication no. 95-3371. (National Toxicology Program technical report series no. 440).

Spektor DM, Lippmann M, Lioy PJ, Thurston GD, Citak K, James D J, Bock N, Speizer FE, Hayes C (1988), Effects of ambient ozone on respiratory function in active, normal children. Am. Rev. Respir. Dis. 137:313-20.

Steenland K, Savitz D, eds (1997). *Topics in Environmental Epidemiology.* Oxford University Press.

Tepper, J S et al. (1994) The relative contribution of concentration and duration to ozone (O_3)-induced lung injury. Research Triangle Park, NC: U. S. Environmental Protection Agency, National Health & Environmental Effects Research Laboratory, Pulmonary Toxicology Branch.

US Department of Health & Human Services, CDC (1997). NIOSH Pocket Guide to Chemical Hazards. June 1997.

US Department of Health and Human Services, CDC (1998). MMWR, Vol. 47/No. SS1, April 24, 1998.

US EPA (1989). US Environmental Protection Agency. Aerometric Information Retrieval System User's Guide (Vol. I), Research Triangle Park, NC: USEPA, Office of Air Quality Planning and Standards, Technical Support Division, National Air Data Branch.

US EPA (1993). US Environmental Protection Agency Regional interim emission inventories (1987-1991), v. II: emission summaries. Research Triangle Park, NC: Office of Air Quality Planning and Standards; report no. EPA-454/R-93-021b. Available from: NTIS, Springfield, VA; PB93-236115

US EPA (19996a). US Environmental Protection Agency. Air Quality Criteria for Ozone and Related Photochemical Oxidants Volume I, II, and III. EPA Report No. EPA/600/P-93/004af-cf.

US EPA (1996b). US Environmental Protection Agency. Review of National Ambient Air Quality Standards for Ozone Assessment of Scientific and Technical Information, OAQPS Staff Paper.

US EPA (1997). US Environmental Protection Agency. Fact Sheet - Health and Environmental Effects of Ground-Level Ozone.

US EPA (1998). US Environmental Protection Agency. Ozone generators that are sold as air cleaners. http://www.epa./iaq/pubs/ozonegen.html

US EPA (1999a). US Environmental Protection Agency. Access to air pollution data. http://www.epa.gov/AIRSData, created 03 August 1999, accessed 16 August 1999.

US EPA (1999b). US Environmental Protection Agency. *Smog-Who Does It Hurt?* Office of Air Quality Planning & Standards.

Weschler, Charles J.; Shields, Helen, C.; and Naik, Datta, V.: Indoor Ozone Exposure. Journal of Air Pollution Control Association 39:1562-1568 (1989).